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Application No.: Confirmation No.:

Applicants: Jean-Louis Henri Dasseux, et al.

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P.O. Box 1450
Alexandria, VA 22313-1450

PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination on the merits, please amend the application as set forth below.

Amendments to the Specification are reflected on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks begin on page 20 of this paper.

Amendments to the Specification:

Please add the following new paragraph on page 1, after the title and before line 4:

This application is a 371 application of PCT/US2003/041448 filed December 24, 2003.

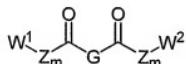
Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1 – 8 (canceled).

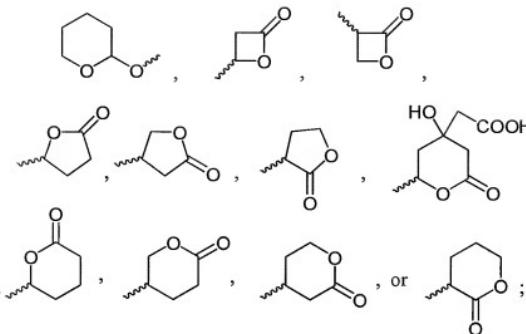
Claim 9 (currently amended): A compound of the formula **Ia**:



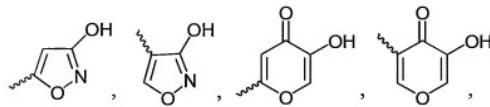
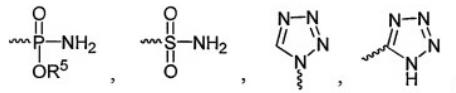
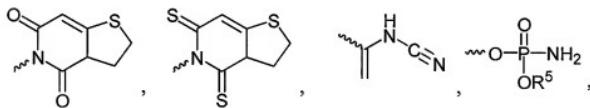
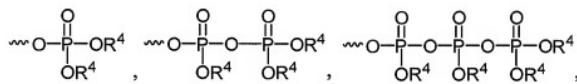
Ia

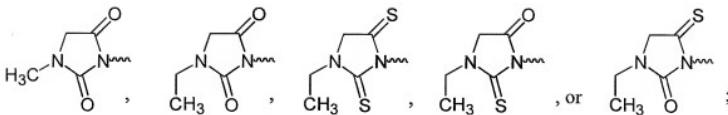
or a pharmaceutically acceptable salt, hydrate, solvate, or a mixture thereof, wherein

- (a) each occurrence of Z is independently CH₂ or CH=CH, wherein each occurrence of m is independently an integer ranging from 1 to 9;
- (b) G is (CH₂)_x, CH₂CH=CHCH₂, or CH=CH, where x is 2, 3, or 4;
- (c) W¹ is L and W² are independently is L, V, or C(R¹)(R²)-(CH₂)_n-Y, where c is 1 or 2;
- (d) each occurrence of R¹ and R² is independently CO₂H, CO₂(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, benzyl, or R¹ and R² and the carbon to which they are both attached are taken together to form a (C₃-C₇)eyeleaky(C₃-C₇)cycloalkyl group;
- (e) L is C(R¹)(R²)-(CH₂)_n-Y, where n is an independent integer ranging from 0 to 4;
- (f) V is



(g) each occurrence of Y is independently (C₁-C₆)alkyl, OH, COOH, CHO, (CH₂)_nCOOR³, SO₃H,





where

- (i) R^3 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, phenyl, or benzyl and is unsubstituted or substituted with one or more halo, OH, (C_1-C_6) alkoxy, or phenyl groups;
- (ii) each occurrence of R^4 is independently H, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, or (C_2-C_6) alkynyl and is unsubstituted or substituted with one or two halo, OH, C_1-C_6 alkoxy, or phenyl groups; and
- (iii) each occurrence of R^5 is independently H, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, or (C_2-C_6) alkynyl; and

provided that:

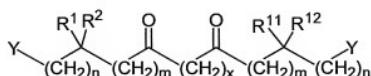
- (i) if x is 4, each occurrence of Z is CH_2 , each occurrence of m is 4, and W^1 is $-CH(CH_3)CO_2H$, then W^2 is not the same as W^1 ;
- (ii) if x is 4, each occurrence of Z is CH_2 , each occurrence of m is 2, and W^1 is $-C(phenyl)_2CH_2CO_2H$, then W^2 is not the same as W^1 .

Claims 10 – 12 (canceled).

Claim 13 (original): The compound of claim 9, wherein W^1 and W^2 are independent L groups.

Claim 14 (original): The compound of claim 13, wherein each occurrence of Y is independently OH, $COOR^3$, or COOH.

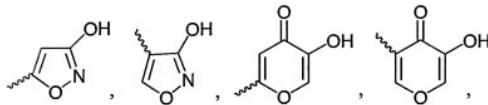
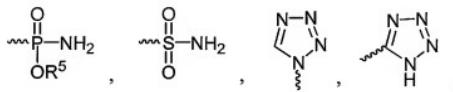
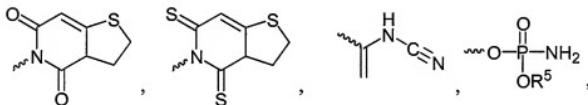
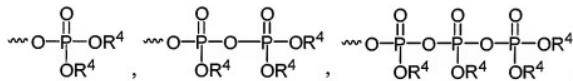
Claim 15 (currently amended): A compound of the formula Ib

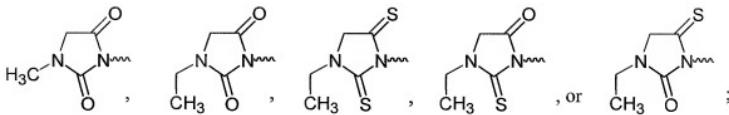


Ib

or a pharmaceutically acceptable salt, hydrate, solvate, or a mixture thereof, wherein:

- (a) each occurrence of m is independently an integer ranging from 1 to 9;
- (b) x is 2, 3, or 4;
- (c) n is an independent integer ranging from 0 to 4;
- (d) each occurrence of R¹ and R² is independently CO₂H, CO₂(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, benzyl, or R¹ and R² and the carbon to which they are both attached are taken together to form a (C₃-C₇)eyeloaky¹ (C₃-C₇)cycloalkyl group;
- (e) each occurrence of R¹¹ and R¹² is independently H, CO₂H, CO₂(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, benzyl, or R¹¹ and R¹² and the carbon to which they are both attached are taken together to form a (C₃-C₇)eyeloaky¹ (C₃-C₇)cycloalkyl group;
- (f) each occurrence of Y is independently (C₁-C₆)alkyl, OH, COOH, CHO, COOR³, SO₃H,





where

- (i) R^3 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, phenyl, or benzyl and is unsubstituted or substituted with one or more halo, OH, (C_1-C_6) alkoxy, or phenyl groups;
- (ii) each occurrence of R^4 is independently H, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, or (C_2-C_6) alkynyl and is unsubstituted or substituted with one or two halo, OH, C_1-C_6 alkoxy, or phenyl groups; and
- (iii) each occurrence of R^5 is independently H, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, or (C_2-C_6) alkynyl;

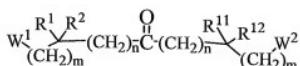
provided that:

- (i) if x is 4 each occurrence of m is 4, and W^1 is $-CH(CH_3)CO_2H$, then W^2 is not the same as W^1 ;
- (ii) if x is 4 occurrence of m is 2, and W^1 is $-C(\text{phenyl})_2CH_2CO_2H$, then W^2 is not the same as W^1 .

Claims 16 (original): The compound of Claim 15, wherein each occurrence of Y is independently OH, COOR^3 , or COOH.

Claims 17 – 19 (canceled).

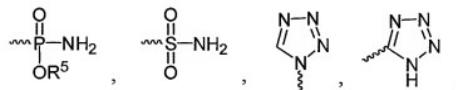
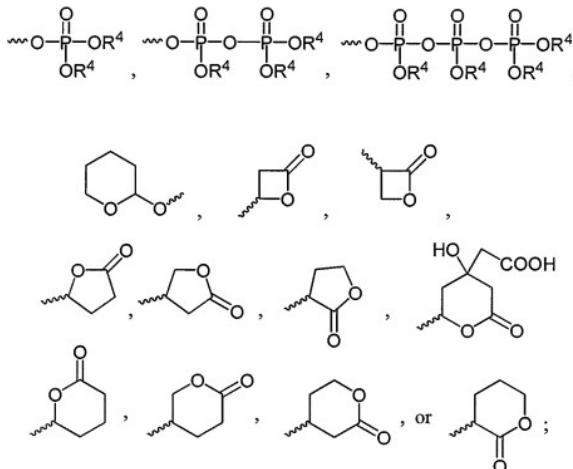
Claim 20 (currently amended): A compound of the formula II:

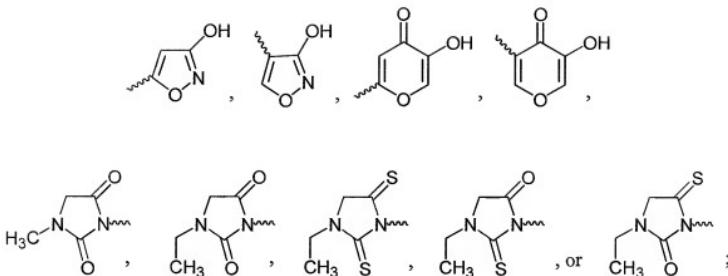


II

or a pharmaceutically acceptable salt, hydrate, solvate, or a mixture thereof, wherein

- (a) R¹ and R² are independently CO₂H, or CO₂(C₁–C₆)alkyl, (C₁–C₆)alkyl, (C₂–C₆)alkenyl, (C₂–C₆)alkynyl, phenyl, or benzyl; or R¹, R², and the carbon to which they are both attached are taken together to form a (C₃–C₇)cycloalkyl group;
- (b) R¹¹ and R¹² are independently CO₂H, CO₂(C₁–C₆)alkyl, (C₁–C₆)alkyl, (C₂–C₆)alkenyl, (C₂–C₆)alkynyl, phenyl, or benzyl; or R¹¹, R¹², and the carbon to which they are both attached are taken together to form a (C₃–C₇)cycloalkyl group;
- (c) n is an integer ranging from 1 to 6;
- (d) each occurrence of m is independently an integer ranging from 0 to 4;
- (e) W¹ and W² are independently (C₁–C₆)alkyl, CH₂OH, C(O)OH, CHO, OC(O)R³, C(O)OR³, SO₃H,

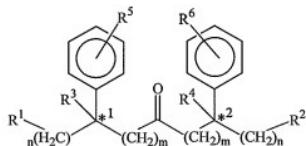




where

- (i) R^3 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, phenyl, or benzyl and is unsubstituted or substituted with one or more halo, OH, (C_1-C_6) alkoxy, or phenyl groups,
- (ii) each occurrence of R^4 is independently H, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, or (C_2-C_6) alkynyl and is unsubstituted or substituted with one or two halo, OH, C_1-C_6 alkoxy, or phenyl groups;
- (iii) each occurrence of R^5 is independently H, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, or (C_2-C_6) alkynyl.

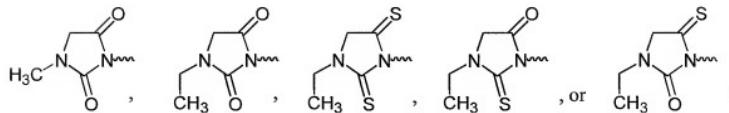
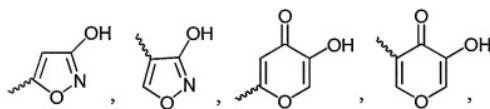
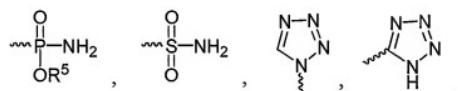
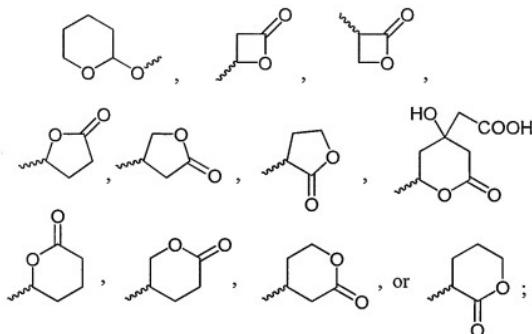
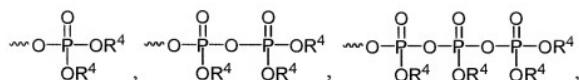
Claim 21 (currently amended): A compound of formula IIa:



IIa

or a pharmaceutically acceptable salt, hydrate, solvate, or a mixture thereof, wherein

- (a) R^1 and R^2 are OH, COOH, CHO, $COOR^7$, SO_3H ,



where

- (ii)(i) R⁷ is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, or benzyl and is unsubstituted or substituted with one or more halo, OH, (C₁-C₆)alkoxy, or phenyl groups,
- (ii) each occurrence of R⁸ is independently H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl and is unsubstituted or substituted with one or two halo, OH, C₁-C₆ alkoxy, or phenyl groups,
- (iii) each occurrence of R⁹ is independently H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl;
- (b) R³ and R⁴ are CO₂H, or CO₂(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, or benzyl;
- (c) R⁵ and R⁶ are hydrogen, halogen, (C₁-C₄)alkyl, (C₁-C₄)alkoxy, (C₆)aryloxy, CN, or NO₂, N(R⁵)₂ where R⁵ is H, (C₁-C₄) alkyl, phenyl, or benzyl;
- (d) each occurrence of m is independently an integer ranging from 1 to 5;
- (e) each occurrence of n is independently an integer ranging from 0 to 4; and
- (f) *¹ and *² represent independent chiral-carbon centers, wherein each center may independently be R or S.

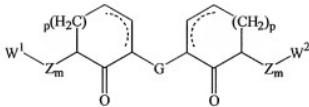
Claim 22 (original): A compound as in claim 21 wherein *¹ is a chiral-carbon center of the stereochemical configuration R or substantially R.

Claim 23 (original): A compound as in claim 21 wherein *¹ is a chiral-center of the stereochemical configuration S or substantially S.

Claim 24 (original): A compound as in claim 21 wherein *² is a chiral-carbon center of the stereochemical configuration R or substantially R.

Claim 25 (original): A compound as in claim 21 wherein *² is a chiral-center of the stereochemical configuration S or substantially S.

Claim 26 (currently amended): A compound of the formula **III**:

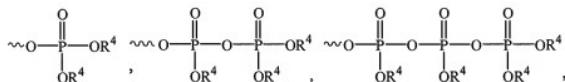


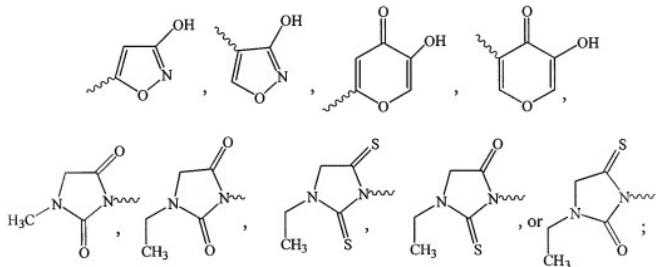
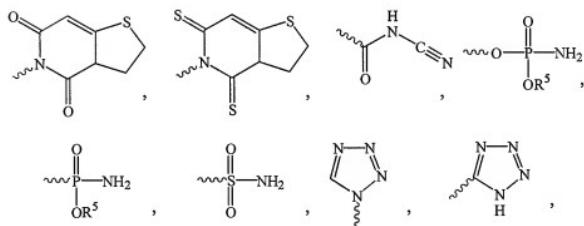
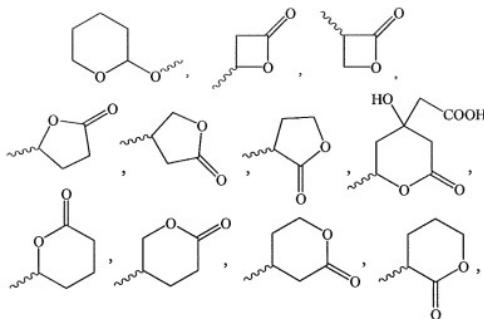
III

or a pharmaceutically acceptable salt, hydrate, solvate, or a mixture thereof,

wherein

- (a) each occurrence of Z is independently CH₂, CH=CH, or phenyl, where each occurrence of m is independently an integer ranging from 1 to 5, but when Z is phenyl then its associated m is 1;
- (b) G is (CH₂)_x, CH₂CH=CHCH₂, CH=CH, CH₂-phenyl-CH₂, or phenyl, where x is an integer ranging from 1 to 4;
- (c) W¹ and W² are independently C(R¹)(R²)-(CH₂)_n-Y where n is an integer ranging from 0 to 4;
- (d) R¹ and R² are independently CO₂H, CO₂(C₁-C₆)alkyl, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, or benzyl or R¹ and R² are both H, or R¹, R¹, and the carbon to which they are both attached are taken together to form a (C₃-C₇)cycloalkyl group;
- (e) Y is (C₁-C₆)alkyl, (CH₂)_nOH, (CH₂)_nCOOH, (CH₂)_nCHO, (CH₂)_nCOOR³, SO₃H,





where

- (+) (i) R³ is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl, phenyl, or benzyl and is unsubstituted or substituted with one or more halo, OH, (C₁-C₆)alkoxy, or phenyl groups,

- (ii) each occurrence of R⁴ is independently H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl and is unsubstituted or substituted with one or two halo, OH, C₁-C₆ alkoxy, or phenyl groups,
 - (iii) each occurrence of R⁵ is independently H, (C₁-C₆)alkyl, (C₂-C₆)alkenyl, or (C₂-C₆)alkynyl; and
- (f) each occurrence of p is independently 2 or 3 where the broken line represents an optional presence of one or more additional carbon-carbon bonds that when present complete one or more carbon-carbon double bonds.

Claim 27 (original): The compound of claim 26, wherein W¹ and W² are independent C(R¹)(R²)-(CH₂)_n-Y groups, where n is an independent integer ranging from 0 to 4, and each occurrence of Y is independently OH, COOR⁴, or COOH.

Claim 28 (original): The compound of claim 26, wherein p is 0.

Claim 29 (original): The compound of claim 26, wherein p is 1.

Claims 30 – 33 (canceled).

Claim 34 (currently amended): A pharmaceutical composition comprising a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 35 (canceled).

Claim 36 (currently amended): A method for treating or preventing a cardiovascular disease in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 37 (currently amended): A method for treating or preventing a dyslipidemia in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 38 (currently amended): A method for treating or preventing a dyslipoproteinemia in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 39 (currently amended): A method for treating or preventing a disorder of glucose metabolism in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 40 (currently amended): A method for treating or preventing Alzheimer's Disease in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 41 (currently amended): A method for treating or preventing Syndrome X or Metabolic Syndrome in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 42 (currently amended): A method for treating or preventing septicemia in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 43 (currently amended): A method for treating or preventing a thrombotic disorder in a patient, comprising administering to a patient in need of such treatment or

prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 44 (currently amended): A method for treating or preventing a peroxisome proliferator activated receptor associated disorder in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 45 (currently amended): A method for treating or preventing obesity in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 46 (currently amended): A method for treating or preventing pancreatitis in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 47 (currently amended): A method for treating or preventing hypertension in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 48 (currently amended): A method for treating or preventing renal disease in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 49 (currently amended): A method for treating or preventing cancer in a patient, comprising administering to a patient in claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 50 (currently amended): A method for treating or preventing inflammation in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 51 (currently amended): A method for treating or preventing impotence in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 52 (currently amended): A method for treating or preventing a neurodegenerative disease or disorder in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 53 (currently amended): A method of inhibiting hepatic fatty acid synthesis in a patient, comprising administering to a patient in need thereof a therapeutically or prophylactically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 54 (currently amended): A method of inhibiting sterol synthesis in a patient, comprising administering to a patient in need thereof a therapeutically or prophylactically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 55 (currently amended): A method of treating or preventing metabolic syndrome disorders in a patient, comprising administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 56 (currently amended): A method of treating or preventing a disease or disorder that is capable of being treated or prevented by increasing HDL levels, which comprises administering to a patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 57 (currently amended): A method of treating or preventing a disease or disorder that is capable of being treated or prevented by lowering LDL levels, which comprises administering to such patient in need of such treatment or prevention a therapeutically effective amount of a compound of claim 1, 9, 15, 18, 20, 21, 26, or 30.

Claim 58 (new): A compound or pharmaceutically acceptable salt, hydrate or solvate thereof selected from:

t-Butyl 1-[9-[1-(tert-butoxycarbonyl)cyclopropyl]-5-oxononyl]-1-cyclopropanecarboxylate,
Diethyl 10-oxo-2,2,18,18-tetramethyl-nonadecanedioate,
11-(1-Carboxycyclopropyl)-2,2-diemethyl-7-oxoundecanoic acid,
1-[9-(1-Carboxycyclopropyl)-5-oxononyl]-1-cyclopropanecarboxylic,
11-(1-Carboxycyclobutyl)-2,2-dimethyl-7-oxoundecanoic acid,
1-[9-(1-Carboxycyclobutyl)-5-oxononyl]-1-cyclobutanecarboxylic acid,
1-[9-(1-Carboxycyclopentyl)-5-oxononyl]-1-cyclopentylcarboxylic acid,
13-(1-Carboxycyclopropyl)-2,2-dimethyl-8-oxotridecanoic acid,
1-[11-(1-Carboxycyclopropyl)-6-oxoundecyl]-1-cyclopropane carboxylic acid,
1-[11-(1-Carboxycyclopentyl)-6-oxoundecyl]-1-cyclopentane carboxylic acid,
10-Oxo-2,2,18,18-tetramethyl-nonadecanedioic acid.

Claim 59 (new): A compound of claim 58 wherein said compound is *t*-Butyl 1-[9-[1-(tert-butoxycarbonyl)cyclopropyl]-5-oxononyl]-1-cyclopropanecarboxylate, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 60 (new): A compound of claim 58 wherein said compound is Diethyl 10-oxo-2,2,18,18-tetramethyl-nonadecanedioate, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 61 (new): A compound of claim 58 wherein said compound is 11-(1-Carboxycyclopropyl)-2,2-diemethyl-7-oxoundecanoic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 62 (new): A compound of claim 58 wherein said compound is 1-[9-(1-Carboxycyclopropyl)-5-oxononyl]-1-cyclopropanecarboxylic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 63 (new): A compound of claim 58 wherein said compound is 11-(1-Carboxycyclobutyl)-2,2-dimethyl-7-oxoundecanoic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 64 (new): A compound of claim 58 wherein said compound is 1-[9-(1-Carboxycyclobutyl)-5-oxononyl]-1-cyclobutanecarboxylic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 65 (new): A compound of claim 58 wherein said compound is 1-[9-(1-Carboxycyclopentyl)-5-oxononyl]-1-cyclopentylcarboxylic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 66 (new): A compound of claim 58 wherein said compound is 13-(1-Carboxycyclopropyl)-2,2-dimethyl-8-oxotridecanoic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 67 (new): A compound of claim 58 wherein said compound is 1-[11-(1-Carboxycyclopropyl)-6-oxoundecyl]-1-cyclopropane carboxylic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 68 (new): A compound of claim 58 wherein said compound is 1-[11-(1-Carboxycyclopentyl)-6-oxoundecyl]-1-cyclopentane carboxylic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

Claim 69 (new): A compound of claim 58 wherein said compound is 10-Oxo-2,2,18,18-tetramethyl-nonadecanedioic acid, or a pharmaceutically acceptable salt, hydrate, or solvate thereof.

REMARKS

I. Priority

In accordance with 35 U.S.C. §119(e) and 35 U.S.C. §120, the Applicants have submitted an amendment containing a specific reference to the prior filed applications in the section above entitled "In the Specification". The Applicants note that a petition and surcharge are not required to correct this priority claim, because the Applicants have amended the first sentence of the specification to contain the specific reference within the later of 4 months from the date on which the National Stage commenced under 35 U.S.C. 371 or 16 months from the filing of the prior filed application.

II. Support for Amendments to Claims

The amendments to the claims find support in the specification or from the original claim set. For example, the amendment to claim 9 wherein W¹ is L finds support in original claim 10. The remaining substantive amendments to claim 9 involved the deletion of subject matter in one claim element (element (d)) in order to place the claim in better condition for examination. Similar types of amendments are made in claims 15, 20, 21, and 26. Various typographical errors are also corrected.

Regarding new claims 58 – 69, the compounds claimed therein correspond to compounds 106d, 106n, 107c, 107d, 107e, 107f, 107g, 107k, 107l, 107m, and 107n disclosed in the specification on pages 232, 236 – 240, 292, and 293. Therefore, no new matter is presented.

Conclusion

The Applicants respectfully request entry of the present amendment.

If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-622-1363.

Respectfully submitted,

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